IN THE NAME OF GOD

BRUGADA SYNDROM 1393

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Autosomal dominant

- Epidemiology:
- Prevalence: ranging from 0.14% in the japanese to 0.61% in europeans & may reach to 3% in southeast Asia.
- In up to 60% of patients ,the disease can be sporadic .
- A FH of unexplained SCD is present in approximately 20% to 40% of BS.

Autosomal dominant triat:men to women(8:1)

- The age of onset of clinical manifestation (syncope or cardiac arrest) is the third to fourth decade of life(mean age of occurrence ,41+_ 15 years.

Clinical presentation

- The patient is high risk of rapid polymorphic VT ,VF and SCD:
- Agonal respirations,nocturnal labored respiration with agitation,and seizures are the only symptoms the patient may have before SCD occurs.

Cardiac arrhythmia and death in the Brugada syndrom seem to occur largely in the early morning hours during sleep and in the setting of bradycardia.

- Some episodes of syncope or SCD can be triggered by fever,large meals (gastric distention),alcohol and cocain toxicity, and drugs.
- In fact,it now appears that many previously described episodes of "febril seizures" may in fact represent bouts of polymorphic VT in patients with temperature-sensitive mutations.

Approximately 20% of patients with BS develop PSVT

- AF is observed in 10% to 20% of patients.
- The identification of concomitant conduction defects(PR interval>210 ms,and HV interval >60 ms) has been shown to correlate with the presence of SCN5A mutations.Therefore,all SCN5A-positive patients should be closely monitored for the onset of conduction block.

ECG

- Type 1:ST elevation of at least 2mm with a coved morphology,incomplete or complete RBBB pattern and followed by a descending negative T wave,with little or no isoelectric separation .
- Type2:saddleback appearance with a high take-off ST segment elevation of at least 2 mm, positive or biphasic T wave.
- Type3:has either a saddleback or coved appearance with an ST segment elevation of less than 1 mm.

These 3 patterns can be observed spontaneously in serial ECG tracings from the same patients or after the introduction of specific drugs

- Type 1 :diagnostic of BS
- Type 2 & 3:suggestive but not specific

- Cephalad placement of the right precordial leads (up to 2th intercostal space above normal)can increase the sensitivity for detecting the BS

QT interval

- A slight prolongation of the QT interval is sometimes observed in association with ST segment elevation in patients with the BS.
- The QT is proloned more in the right precordial leads than it is in the left precordial leads,presumably because of a preferential prolongation of action potential duration in right ventricular epicardium secondary to accentuation of the action potential notch.

Epsilon-like waves and localized prolongation of the QRS in the right precordial leads have been observed insome patients with a spontaneous or drug-induced type I BS,likely reflecting RV activation delay.

- SAECG:late potentials in 60% to 70% of clinically affected BS .
- ETT:can potentially aggrevate the ECG abnormalities in the BS,including widening of the QRS,prolongation of the QTc duration

Diagnosis of the BS

- Criteria:
- Type 1 ST elevation in more than one right precordial lead ,in conjunction with one of following :
- 1.documanted VF ;2.polymorphic VT;
- 3.FH of SCD at age less than 45 years
- 4.coved-type ECG in family members
- 5.inducibility of VT with PES
- 6.syncope; 7.nocturnal agonal respiration

BS is considered positive when type 2 or type 3 can conversion to the type 1 after drug .
One or more of the clinical criteria should be present

Provocative Drug Testing

- Administration of :Ajmalin,Flecainide,Procainamide
- Test is terminated when:1. type 1 developes
- 2.ST elevation in type 2 increases by at least 2 mm 3.PVC or other arrythmia develop
- 4.QRS widens by 30% or more
- Isoproterenol and Sodium lactate can be effective antidotes

Genetic Testing

- Negative results of genetic testing does not exclude the presence of the disease
- BS is a channelopathy that causes current dysfunction in those channels participating in the generation of the cardiac action potential.
- SCN5A is the first gene linked to BS

Mechanism of BS ECG pattern

- The cellular basis is though to be the result of loss of function of Na+ channels(reduced I_{Na}) that differentially alters the action potential morphology in epicardial versus endocardial cells.

- The excessive increase in intramural dispersion of repolarization(between epicardium and endocardium) facilitates reentrant exitation waves between depolarized endocardium and prematurely repolarized epicardium.
- RVOT is the critical ares and is a frequent origin of VT and VF

Quinidine

- In addition to blocking I_{Na} ,has a relatively strong effect in blocking I_{to} .Hence,quinidine can effectively suppress ST elevation and ventricular arrythmia in patients with the BS.
- Beta-adrenergic stimulation induces increased inward I_{CaL} ,and attenuates the excess of outward current,resulting in reduction of ST elevation .(Isoproterenol)

Drugs can unmask BS

- Verapamil,lithium,H1 antihistamines,propofol,
- Alcohol intoxication,cocain intoxication.
- Vagomimetic agents,beta blockers

Risk Stratification

- Male gender , Spontaneous occurrence of type 1 >>>>higher risk for cardiac events
- Asymptomatic Pts. In whom ST elevation appeared only after drug test >>>low risk

Pts. Presented with aborted SCD>>>>Grim prognosis

- FH of SCD at age < 45y/o , coexistence of early repolarization in the inferolateral leads >>>>poor outcome

Management

- ICD
- For asymptomatic patients with normal baseline ECG and those with spontaneous type I Brugada ECG but noninducible VT/VF during PES ,reassurance is adequate management.

Catheter Ablation

- Monomorphic PVCs originated in the RVOT or RV Purkinje network are often the trigger for VT, and focal RF ablation of the PVCs can be valuable in reducing the burden of arrhythmias and ICD therapies.
- Extensive ablation over the RVOT epicardium can revert the ECG pattern to normal and eliminate episodes of VT/VF.

Pharmacological therapy

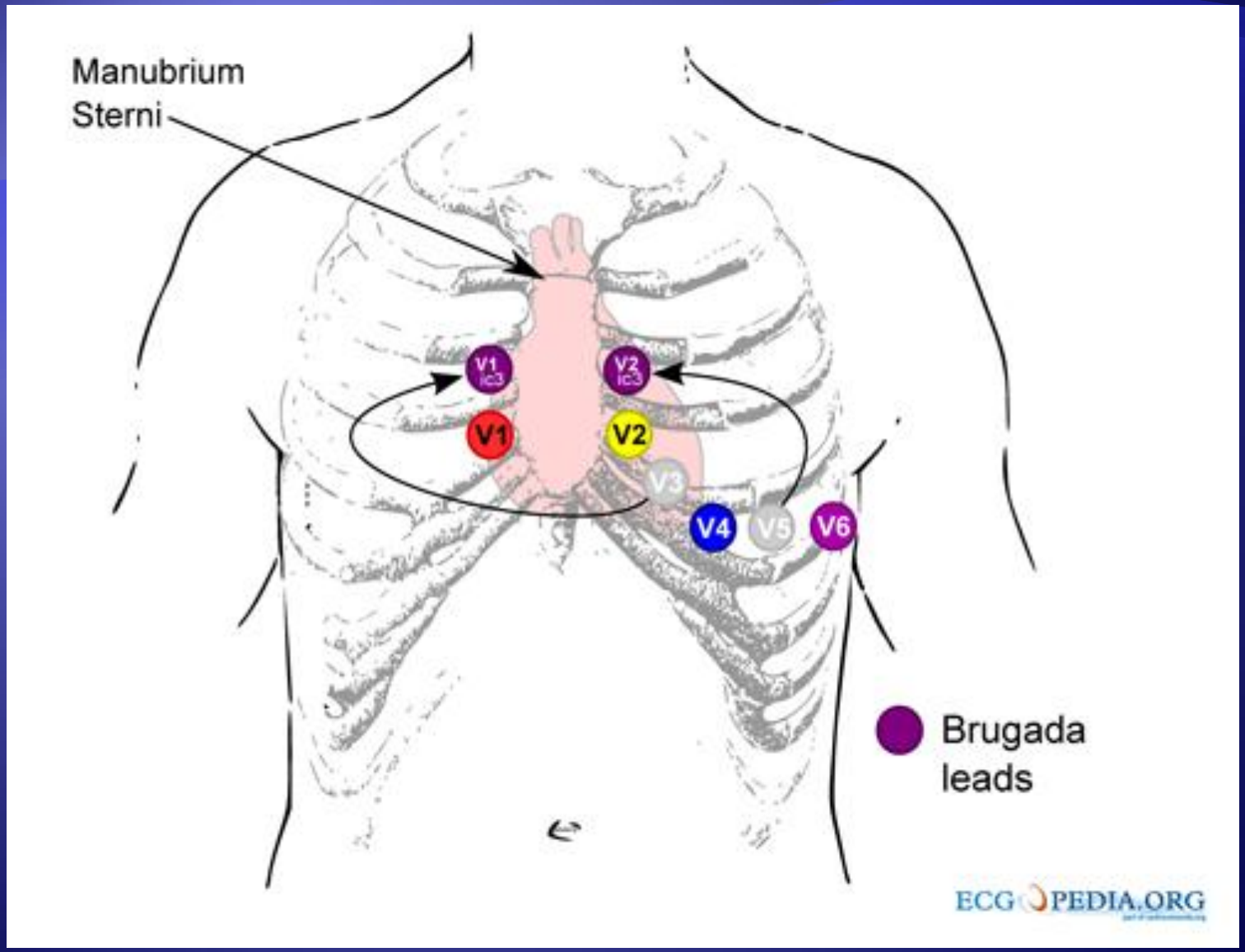
- Quinidine :high dose(1200 – 1500 mg/day)
- Denopamin :an alpha/beta-adrenergic stimulant
- Cilostazol :a phosphodiesterase III inhibitor that increases Ical ,
- Bepridil :was shown to suppress the incidence of VF episodes,probably by blocking Ito.

Electrical storm of VF

- Isoproterenol

Drugs should be avoided

- Antiarrhythmic (class IA,IC)
- Betablockers
- Ttricyclic antidepressants
- Propofol
- K+ channel activators(pinacidil)
- Lithium
- Cocain
- Alpha-adrenergic agonist(methoxamin)
- Vagomimetic agents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Sterni
V1
ic3
V2
ic3
V1
V2
V3
V4
V5
V6
Brugada
leads
ECG PEDIA.ORG

Short QT syndrom

- Inherited channelopathy
- Occuring in young individuals with structurally normal heart
- Short QT(QTc <320 ms) associated with AF,syncope,and/or SCD

Epidemiology

- Majority of affected subjects :men
- Age: variable,from infancy to the 8 decade of life,with a mean age of 20-30 y

- Cardiac arrest is the first clinical manifestation in 1/3 of patients.
- Syncope(14%)
- AF (30%)

- Cardiac arrest has occurred both at rest and under stress

QT less than 320 ms

- Extreme abbreviation of the J_{point}-T_{peak} interval
- (<120 ms)can help distinguish patients with SQTS from healthy subjects with an apparent abbreviation of the ST and shortened QT(mean J_{point}-T_{peak} interval of 188 ms.
- High-amplitude,narrow,symmetrical T waves in the precordial leads

Diagnostic criteria

- QTc
- <370 1
- <350 2
- <330 3
- Jpoint-Tpeak <120 1

Clinical history

- H/O SCA 2
- Documented polymorphic VT or VF 2
- Unexplained syncope 1
- AF 1

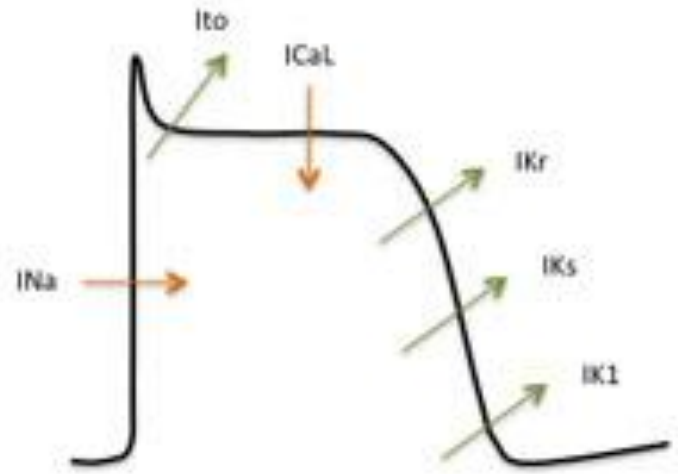
Family history

- 1th or 2ed –degree ,high probability SQTS 2
- 1th or 2ed –degree,autopsy-neg.SCD 1
- Sudden infant death syndrom 1

- Genotype
- Positive 2
- Mutation in culprit gene 1

High probability SQTS: >=4

- Intermediate probability :3
- Low propability:<=2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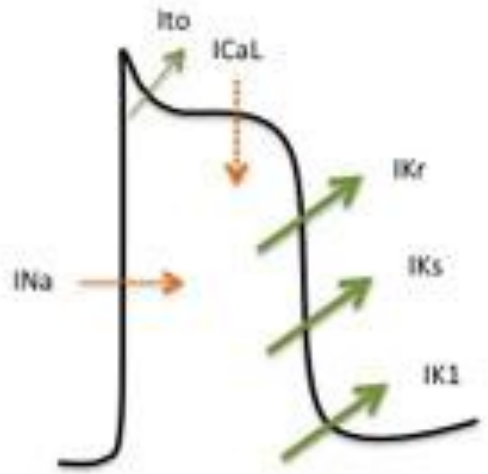
Ito
ICaL
IKr
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IK1

	Gene	Current	Phenotype
SQT1	KCNH2	IKr	
SQT2	KCNQ1	IKs	
SQT3	KCNJ2	IK1	
SQT4	CACNA1C	ICaL	
SQT5	CACNB2B	ICaL	


I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6

The presence of short QT interval on the surface ECG is not sufficient to make a diagnosis of SQTS and does not imply a significant risk of SCD

- Other etiologies for shortening of the QT interval should be excluded,including :
- -kyperkalemia
- -hypercalcemia
- -hyperthermia
- -acidosis
- -dig.overdoses
- -administration of acetylcholine and catecholamines

Management

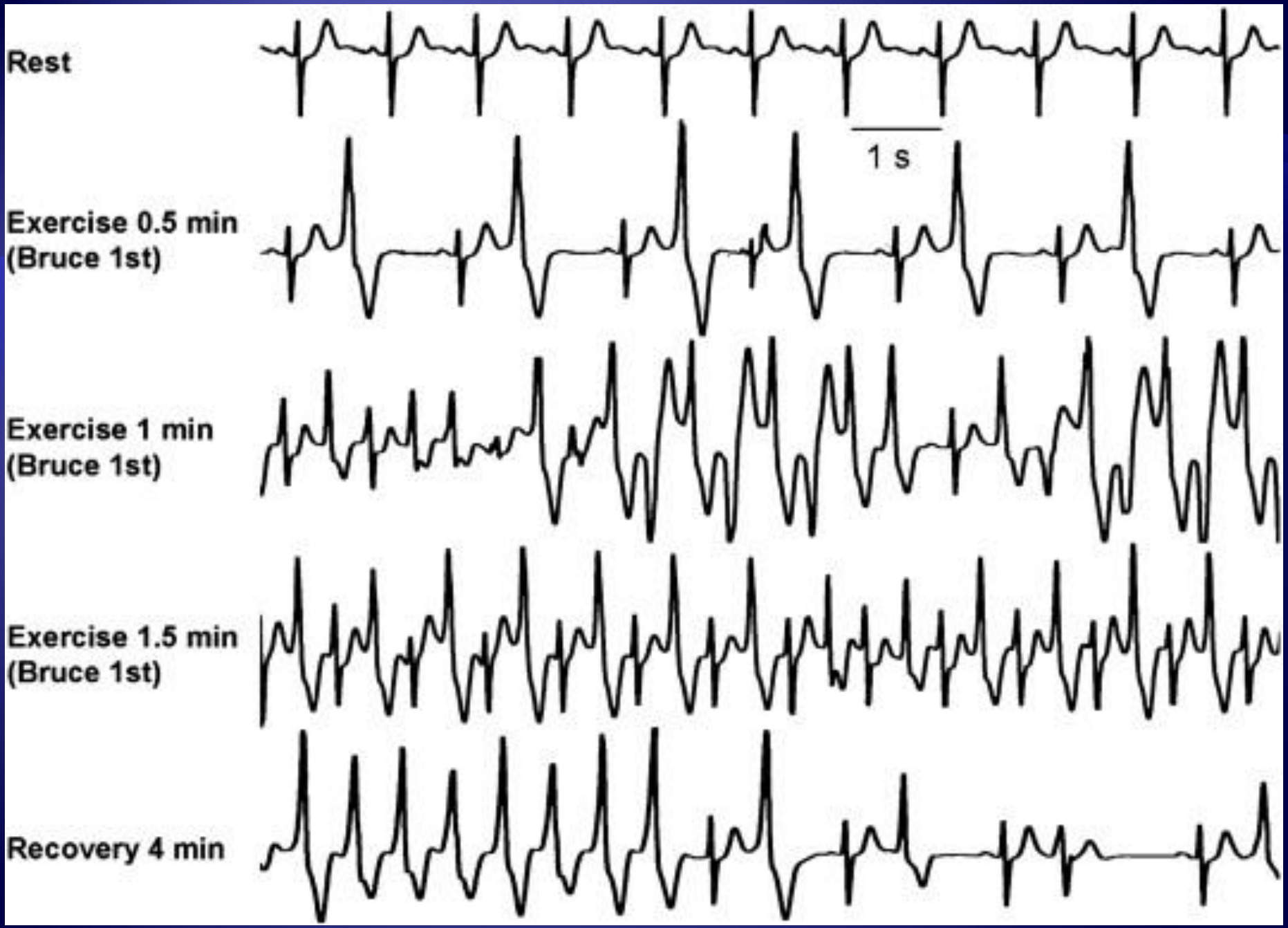
- ICD
- quinidine

Catecholaminergic polymorphic VT(CPVT)

- Familial polymorphic VT
- Rare
- Highly malignant
- Inherited arrhythmia disorder
- Exercise-and stress-induced polymorphic or bidirectional VT
- Structurally normal heart

Prevalence : 1:10000

- Mean age of onset:7-9y
- Approximately 30% ,have a F/H of stress-related syncope,seizure,SCD before age 40y.
- There is a high level of penetrance of the disease (75% to 80%)


Rest
1 s
Exercise 0.5 min
(Bruce 1st)
Exercise 1 min
(Bruce 1st)
Exercise 1.5 min
(Bruce 1st)
Recovery 4 min

A standard ETT is the most important step foe diagnosis of CPVT

- Isoproterenol
- Holter monitoring
- Invasive EP testing is of no value in the diagnosis or risk stratification
- Genetic testing(cardiac Ryanodine receptor gene RyR2)

Abnormality in the control of sarcoplasmic reticulum Ca2+ release constitute the central pathogenic abnormality in CPVT.

- Sarcoplasmic reticulum load is normal,there is no Ca2+leak.Under beta-areneergic(sympathetic) stimulation,sarcoplasmic reticulum Ca2+ concentration becomes elevated above the reduced threshold,causing Ca2+ to leak out of the sarcoplasmic reticulum.

DADs and triggered activity ,as the arrhythmogenic mechanism

- Mechanism of the bidirectinal morphology of VT is not clear

Management

- Betablockers:nadolol 1 to 2.5 mg/kg /d or propranolol 2.5-3.5 mg/kg/d
- IV propranolol for acute management
- Addition of flecainide to betablocker(flecainide effects are mediated by direct blockade of RyR2 channels and reduction of Ca2+ spark amplitude rather than Na+channel blockade
- Verapamil (an inhibitor of RyR2)
- ICD
- Catheter ablation(monomorphic PVCs)
  left cardiac sympathetic denervation

Early Repolarization Syndromes